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Michael O. Leavitt, Administrator
U.S. Environmental Protection Agency
Ariel Rios Building, 1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on the HPV Test Plan for N,N,N',N',-tetramethylethylenediamine

Dear Administrator Leavitt:

The following comments on the Crompton Corporation's test plan for the chemical N,N,N',N',-tetramethylethylenediamine are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

Crompton submitted its test plan on August 27, 2003, for the chemical N,N,N',N',-tetramethylethylenediamine, (TMEDA) (CAS # 110-18-9), an aliphatic amine used in the preparation of epoxy curing agents and various other chemical manufacturing processes. Crompton has utilized a structure-activity modeling program, ECOSAR, to estimate toxicity to fish and other aquatic organisms. Crompton does not propose testing for the aquatic toxicity endpoints because the predicted values are considered appropriately valid. We commend this approach for estimating ecotoxicity.

At this time, however, we would like to point out that this test plan is very brief and lacks necessary details. Specifically, Crompton does not mention the location or process by which this chemical is made, nor is the potential for human or environmental exposure addressed in this test plan.

We are also concerned that little attempt has been made to categorize TMEDA with similar compounds. TMEDA, as Crompton points out in their ECOSAR analysis, belongs to the aliphatic amine class. With a simple TOXLINE search, we were able to locate dozens of chemicals belonging to that category, many of them HPV chemicals. The first of hundreds of entries, Greim et al. (1998) reviews the toxicological properties of aliphatic amines and presents data on 37 chemicals, including their metabolism, acute, subacute, subchronic, and chronic toxicity, genotoxicity, carcinogenicity and reproductive toxicity, among other effects. Crompton's proposal of a combined repeated dose/reproductive/developmental test (OECD 422) is premature because it fails to examine any existing data on analogous chemicals. This test alone will result in the death

of at least 675 animals. We recommend that Crompton identify the compounds that can be expected to be of similar toxicity to this chemical, as data for similar chemicals may be used to bridge data gaps for repeated dose, reproductive, and developmental toxicity endpoints. HPV participants have been urged to use this approach to reduce the number of animals killed in the HPV program, as indicated in the October 1999 letter and the December 2000 *Federal Register* notice. It states that "[p]articipants shall maximize the use of existing and scientifically adequate data to minimize further testing," and that "[p]articipants shall maximize the use of scientifically appropriate categories of related chemicals and structure activity relationships."

Thank you for your attention to these comments. We can be reached at 202-686-2210, ext. 335 or by email at *kstoick@pcrm.org*.

Sincerely,

Kristie Stoick, M.P.H.
Research Analyst

Chad Sandusky, Ph.D.
Director of Research

Reference:

Greim, H., D. Bury, H-J. Klimisch, M. Oeben-Negele, and K. Ziegler-Skylakakis. (1998) Toxicity of Aliphatic Amines: Structure-Activity Relationship. *Chemosphere* **36(2):** 271-295.